

What is claimed is:

1. A method for treating atherosclerosis which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of an aP2 inhibitor.
2. The method as defined in Claim 1 wherein the aP2 inhibitor binds to the aP2 protein and inhibits its function and/or its ability to bind free fatty acids.
3. The method as defined in Claim 1 wherein the aP2 inhibitor contains a hydrogen bond donator or acceptor group and interacts directly or through an intervening water molecule either by ionic or hydrogen bonding interactions, with one, two, or three of the three amino acid residues, designated as Arg 106, Arg 126 and Tyr 128 in human aP2 within the aP2 protein.
4. The method as defined in Claim 3 wherein the hydrogen bond donator or acceptor group is acid in nature.
5. The method as defined in Claim 3 where said aP2 inhibitor contains an additional substituent which binds to (in) and/or interacts with a discrete pocket within the aP2 protein defined roughly by the amino acid residues Phe 16, Tyr 19, Met 20, Val 23, Val 25, Ala 33, Phe 57, Thr 74, Ala 75, Asp 76, Arg 78 in human aP2.
6. The method as defined in Claim 5 wherein said additional substituent in said aP2 inhibitor is hydrophobic in nature.
7. The method as defined in Claim 5 in which the through space distance from the hydrogen bond donor/acceptor group and the additional substituent group in said aP2 inhibitor is within the distance of about 7 to about 15 Angstroms.
8. The method as defined in Claim 1 wherein Type II diabetes is treated.

9. The method as defined in Claim 1 wherein the aP2 inhibitor is employed in the form of a pharmaceutically acceptable salt thereof or a prodrug ester thereof.

10. The method as defined in Claim 1 wherein the aP2 inhibitor includes an oxazole or analogous ring, a pyrimidine derivative or a pyridazinone derivative.

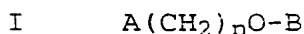
11. The method as defined in Claim 10 wherein the aP2 inhibitor is a substituted benzoyl or biphenyl-2-oxazole-alkanoic acid derivative, an oxazole derivative, a 2-thio-4,5-diphenyloxazole S-derivative, a phenyl-heterocyclic oxazole derivative, a diaryloxazole derivative, a 4,5-diphenyloxazole derivative, an oxazole carboxylic acid derivative, a phenyloxazolyloxazole derivative, or a 2-(4,5-diaryl)-2-oxazolyl substituted phenoxyalkanoic acid derivative.

12. The method as defined in Claim 10 wherein the aP2 inhibitor is a 2-benzyloxypyrimidine derivative, a dihydro(alkylthio)(naphthylmethyl)oxypyrimidine derivative, a thiouracil derivative, or an  $\alpha$ -substituted pyrimidine-thioalkyl or alkyl ether derivative.

13. The method as defined in Claim 10 wherein the aP2 inhibitor is a pyridazinone acetic acid derivative.

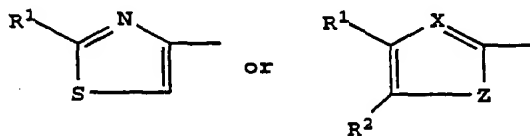
14. The method as defined in Claim 10 wherein the aP2 inhibitor is

(I) a substituted benzoylbenzene or biphenyl alkanoic acid derivative having the structure:



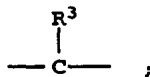
wherein

A is a group having the formula

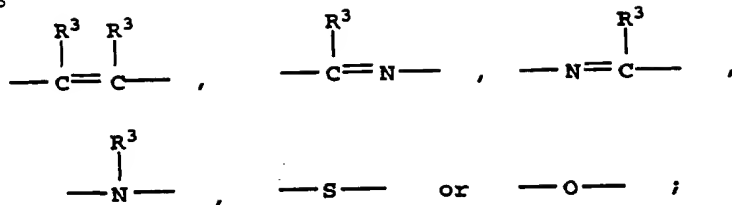


wherein

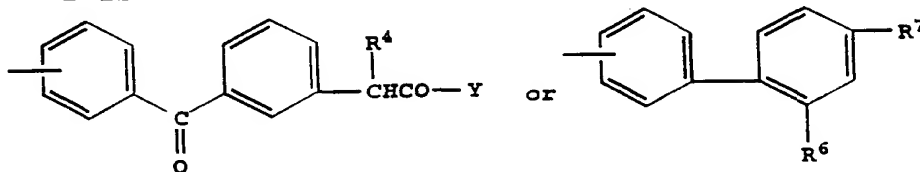
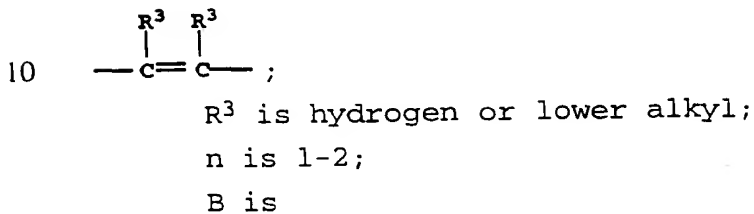
X is -N- or



Z is



5           R<sup>1</sup> is hydrogen, lower alkyl or phenyl;  
          R<sup>2</sup> is hydrogen or lower alkyl; or  
          R<sup>1</sup> and R<sup>2</sup> taken together form a benzene ring, with  
the proviso that when X is -N-, Z is other than



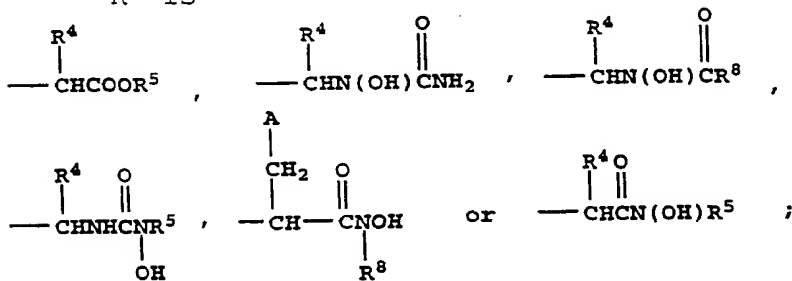
15 wherein

Y is  $OR^5$  or  $N(OH)R^8$ ;

R<sup>4</sup> and R<sup>5</sup> are each, independently, hydrogen or lower alkyl;

R<sup>6</sup> is hydrogen, halo or nitro;

20  $R^7$  is



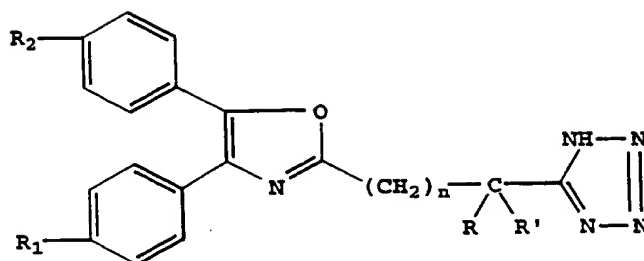
R<sup>8</sup> is lower alkyl;

m is 0-3;

25 or a pharmacologically acceptable salts thereof;

(II) oxazole derivatives which have the structure

II



in which;

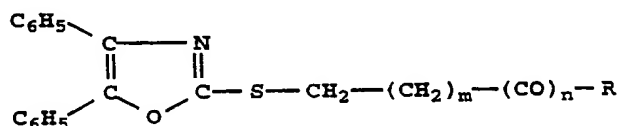
R and R' are identical or different and represent a hydrogen atom or an alkyl radical containing 1 or 2 carbon atoms,

R<sub>1</sub> and R<sub>2</sub> are identical or different and represent hydrogen or halogen atoms or alkyloxy radicals in which the alkyl portion contains 1 to 4 carbon atoms in a straight or branched chain, and

n equals 3 to 6, as well to their salts;

(III) 2-thiol-4,5-diphenyloxazole S-derivatives which have the structure

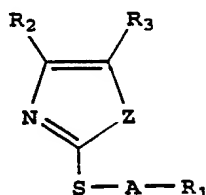
III



wherein m is 0, 1 or 2, n is 1 and R represents hydroxy, alkoxy or amino, and pharmaceutically acceptable addition salts thereof;

(IV) azole derivatives of the structure

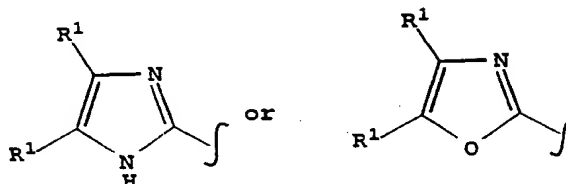
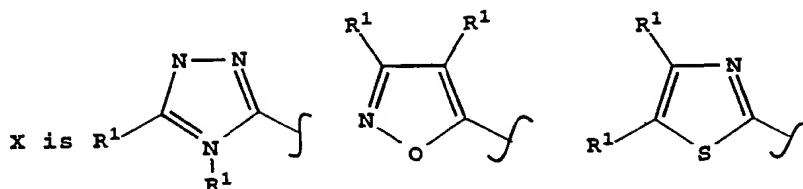
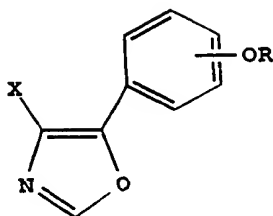
IV



wherein R<sub>1</sub> is carboxyl, esterified carboxyl or other functionally modified carboxyl group; R<sub>2</sub> and R<sub>3</sub> each are aryl of up to 10 carbon atoms; A is C<sub>n</sub>H<sub>2n</sub> in which n is an integer from 1 to 10, inclusive; and Z is O or S, and physiologically acceptable salts thereof;

(V) phenyl-heterocyclic oxazole derivatives which have the structure

V



R is  $\text{CH}_2\text{R}^2$ ;

$\text{R}^1$  is Ph or Th;

$\text{R}^2$  is



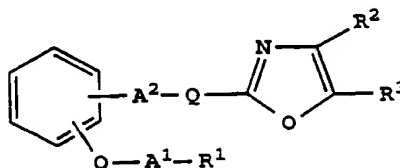
$\text{CO}_2\text{R}^3$ ; and

$\text{R}^3$  is H, or  $\text{C}_1\text{-C}_4$  lower alkyl;

or pharmaceutically acceptable salt thereof;

(VI) diaryloxazole derivatives having the structure

VI



wherein  $\text{R}^1$  is carboxy or protected carboxy,

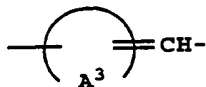
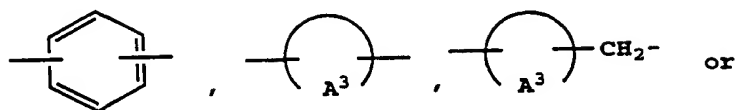
$\text{R}^2$  is aryl,


$\text{R}^3$  is aryl,

$\text{A}^1$  is lower alkylene,

A<sup>2</sup> is bond or lower alkylene and

-Q- is

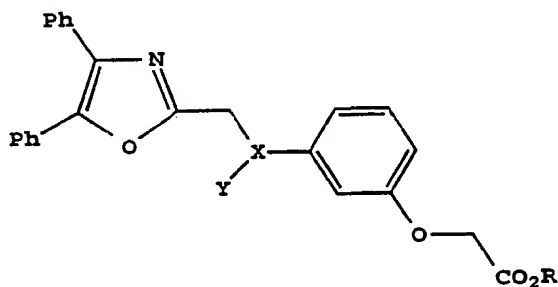


(in which  is cyclo (lower)alkane or cycle(lower)alkene,

each of which may have suitable substituent(s));

(VII) 4,5-diphenyloxazole derivatives having the structure

VIIA



wherein

R is H or C<sub>1</sub>-C<sub>5</sub> lower alkyl,

X is N or CH,

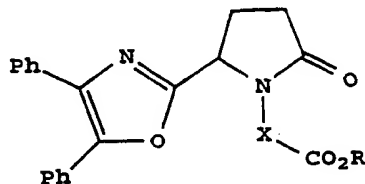
Y is H or CO<sub>2</sub>R<sup>1</sup>, or COR<sup>2</sup>, provided that when X is CH,

Y is not H,

R<sup>1</sup> is C<sub>1</sub>-C<sub>5</sub> lower alkyl, or phenylmethyl, and

R<sup>2</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl;

VIIB



wherein

R is H or C<sub>1</sub>-C<sub>5</sub> lower alkyl,

X is  $(CH_2)_n$  or para or meta substituted phenyl  
wherein the substituent is  $OR^2$ ,

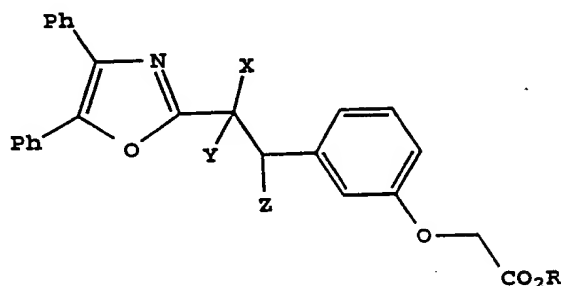
$R^2$  is  $C_1-C_5$  alkyl, and

n is an integer of 4 to 8,

5 and pharmaceutically acceptable salts thereof;

(VIII) oxazole carboxylic acid derivatives having  
the structure

VIII



10

wherein

Y and Z are independently hydrogen or together form  
a bond;

X is CN,  $CO_2R^1$  or  $CONR^2R^3$ ;

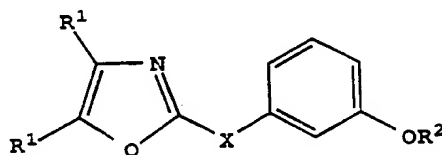
15 R and  $R^1$  are independently or together H, Na, or  
 $C_1-C_5$  lower alkyl;

$R^2$  and  $R^3$  are independently or together H, or  $C_1-C_5$   
lower alkyl;

or alkali metal salt thereof;

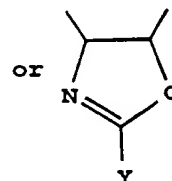
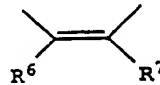
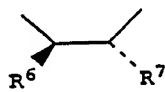
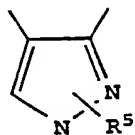
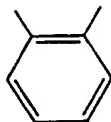
20 (IX) phenyloxazolyloxazole derivatives having the  
structure

IX



wherein

X is



25

Y is CH<sub>3</sub>, Ph, or OH, provided that when Y is OH, the compound exists in the keto-enol tautomerism form



R<sup>1</sup> is Ph or Th;

R<sup>2</sup> is CH<sub>2</sub>R<sup>3</sup>;

R<sup>3</sup> is CO<sub>2</sub>R<sup>4</sup>;

R<sup>4</sup> is H or C<sub>1</sub>-C<sub>5</sub> lower alkyl;

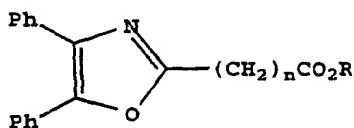
R<sup>5</sup> is H or CH<sub>3</sub>; R<sup>6</sup> is OHCHN or H<sub>2</sub>N; and

R<sup>7</sup> is H or OH;

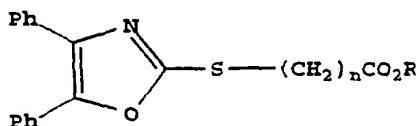
or pharmaceutically acceptable salt thereof;

(X) 2-(4,5-diaryl)-2-oxazolyl substituted phenoxyalkanoic acids and esters having the structure

XA

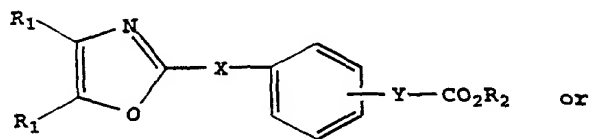


XB

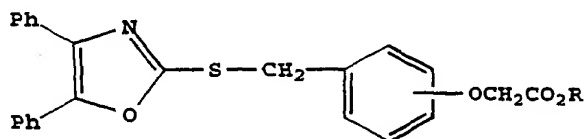


(wherein n is 7-9 and R is hydrogen or lower alkyl; or when R is hydrogen, the alkali metal salt thereof),

XC



XD



wherein

R<sub>1</sub> is phenyl or thienyl;

0905235-071304  
FOET 20-52250660

$R_2$  is hydrogen, lower alkyl or together with  $CO_2$  is tetrazol-1-yl;

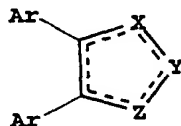
X is a divalent connecting group selected from the group consisting of  $CH_2CH_2$ ,  $CH=CH$ , and  $CH_2O$ ;

- 5 Y is a divalent connecting group attached to the 3- or 4-phenyl position selected from the group consisting of  $OCH_2$ ,  $CH_2CH_2$  and  $CH=CH$ ,

or when  $R_2$  is hydrogen, an alkali metal salt thereof;

- (XI) substituted 4,5-diaryl heterocycles having the  
10 formula

XI



in which

- each group Ar is the same or different and is  
15 optionally substituted phenyl or optionally substituted heteroaryl;

X is nitrogen or  $CR^1$ ;

Y is nitrogen,  $N(CH_2)_nA$  or  $C(CH_2)_nA$ ;

- Z is nitrogen, oxygen or  $N(CH_2)_nA$ , and the dotted  
20 line indicates the optional presence of a double bond so as to form a fully unsaturated heterocyclic ring;

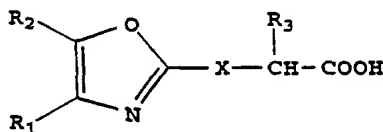
$R^1$  is hydrogen,  $C_{1-4}$ alkyl, optionally substituted phenyl or optionally substituted heteroaryl;

n is 4 to 12; and

- 25 A is  $CO_2H$  or a group hydrolysable to  $CO_2H$ , 5-tetrazolyl,  $SO_3H$ ,  $P(O)(OR)_2$ ,  $P(O)(OH)_2$ , or  $P(O)(R)(OR)$  in which R is hydrogen or  $C_{1-4}$ alkyl, or a pharmaceutically acceptable salt thereof;

(XII) compounds which have the structure

- 30 XII



Where X is O or S;

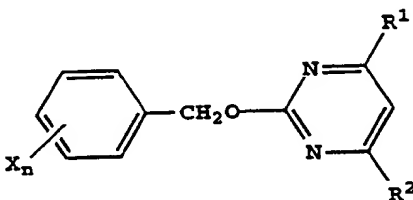
$R_1$  is H, phenyl or phenyl substituted with F, Cl or Br or alkoxy,

$R_2$  is H, alkyl, phenyl or phenyl substituted with F, Cl or Br or alkoxy, and

5  $R_3$  is H or alkyl;

(XIII) 2-benzyloxypyrimidine derivatives having the following structure

XIII



10 wherein

$R^1$  and  $R^2$  are each independently H, a halogen, hydroxyl,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  haloalkyl,  $C_3$ - $C_5$  alkenyl,  $C_3$ - $C_5$  alkynyl,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  haloalkoxy,  $C_3$ - $C_5$  alkenyloxy,  $C_3$ - $C_5$  alkynyloxy,  $C_1$ - $C_4$  alkylthio, or phenyl, with the

15 proviso that at least one of  $R^1$  and  $R^2$  must be hydroxyl;

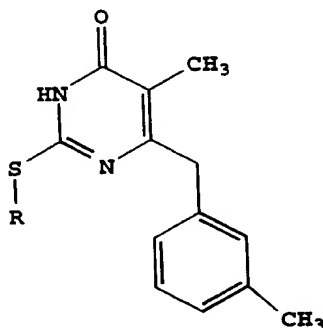
$n$  is an integer of 0 to 5; and

each  $X$  which may be identical or different if  $n$  is greater than 1, is a halogen,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  haloalkyl,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkylthio,  $C_7$ - $C_9$  aralkyloxy, phenyl,

20 hydroxymethyl, hydroxycarbonyl,  $C_1$ - $C_4$  alkoxycarbonyl, or nitro;

(XIV) dihydro(alkylthio)-(naphthylmethyl)-oxypyrimidines which have the structures

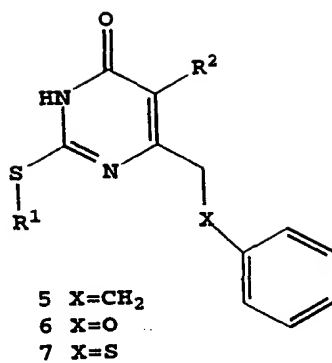
XIVA



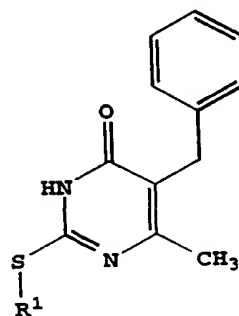
3a R=sec-butyl  
3b R=cyclopentyl  
3c R=cyclohexyl

25

XIVB

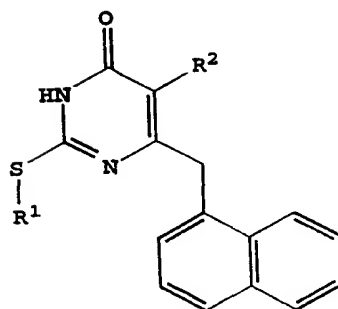


XIVC

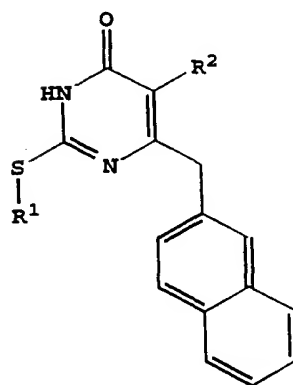


5

XIVD



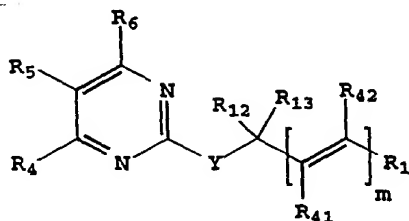
XIVE



R<sup>1</sup> = sec-butyl, cyclopentyl, cyclohexyl;  
10 R<sup>2</sup> = H, CH<sub>3</sub>, including tautomers of the above;

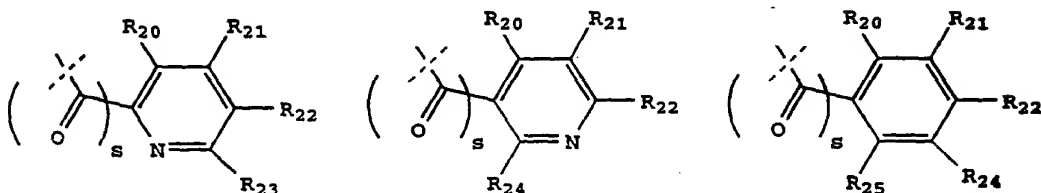
(XVI)  $\alpha$ -substituted pyrimidine-thioalkyl and alkylether compounds which have the structure

XVI



5 where m is 0 or 1;

R<sup>1</sup> is selected from -CO<sub>2</sub>R<sub>53</sub>, -CONR<sub>54</sub>R<sub>55</sub>,



10 where s is 0 or 1, and R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>24</sub>, and R<sub>25</sub> are the same or different and are selected from -H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkenyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -CF<sub>3</sub>, -NO<sub>2</sub>, -halo, -OH, -CN, phenyl, phenylthio, -styryl, -CO<sub>2</sub>(R<sub>31</sub>), -CON(R<sub>31</sub>)(R<sub>32</sub>), -CO(R<sub>31</sub>), -  
15 (CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>), -C(OH)(R<sub>31</sub>)(R<sub>33</sub>), -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(CO(R<sub>33</sub>)), (CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(SO<sub>2</sub>(R<sub>33</sub>)), or where R<sub>20</sub> and R<sub>21</sub>, or R<sub>21</sub> and R<sub>22</sub>, or R<sub>22</sub> and R<sub>23</sub> are taken together to form a five or six-membered saturated or unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-  
20 C<sub>6</sub> alkoxy, -OH, -CH<sub>2</sub>OH, -(CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>), -C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -CF<sub>3</sub>, -halo, CO<sub>2</sub>(R<sub>31</sub>), -CON(R<sub>31</sub>)(R<sub>32</sub>), -CO(R<sub>31</sub>), -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(CO(R<sub>33</sub>)), -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(SO<sub>2</sub>(R<sub>33</sub>)), -CN, -CH<sub>2</sub>CF<sub>3</sub> or -CH(CF<sub>3</sub>)<sub>2</sub>, or phenyl and the saturated ring may be optionally substituted with 1, 2 or 3, -C<sub>1</sub>-C<sub>6</sub> alkyl, -C<sub>1</sub>-C<sub>6</sub>  
25 alkoxy, -OH, -CH<sub>2</sub>OH or -(CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>) or one oxo (=O);

where n is 0-3 and R<sub>31</sub>, R<sub>32</sub> and R<sub>33</sub> are the same or different and are selected from

-H,

C<sub>1</sub>-C<sub>6</sub> alkyl,

phenyl optionally substituted with 1, 2 or 3 -halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -CF<sub>3</sub>, -OH or -CN,

or where R<sub>31</sub> and R<sub>32</sub> taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl, -4-(1-C<sub>1</sub>-C<sub>6</sub>alkyl)piperazinyl, or a member selected from

1-cyclohexenyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-imidazolyl, 4-imidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzimidazolyl, 2-oxazolyl, 4-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 5-methyl-3-isoxazolyl, 5-phenyl-3-isoxazolyl, 4-thiazolyl, 3-methyl-2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-methyl-2-pyrazinyl, 5-chloro-2-thienyl, 3-furyl, benzofuran-2-yl, benzothien-2-yl, 2H-1-benzopyran-3-yl, 2,3-dihydrobenzopyran-5-yl, 1-methylimidazol-2-yl, quinoxalin-2-yl, piperon-5-yl, 4,7-dichlorobenzoxazol-2-yl, 4,6-dimethylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 2,4-dimethylpyrimidin-6-yl, 2-methylpyrimidin-4-yl, 4-methylpyrimidin-6-yl, 6-chloropiperon-5-yl, 5-chloroimidazol[1,2-a]pyridin-2-yl, 1-H-inden-3-yl, 1-H-2-methyl-inden-2-yl, 3,4-dihydronaphth-1-yl, S-4-isopropenylcyclohexen-1-yl or 4-dihydronaphth-2-yl;

where R<sub>53</sub> is selected from -H, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, phenyl (optionally substituted with 1, 2, or 3 -halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -CF<sub>3</sub>, -OH, -CN), or a five or six-membered unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with -H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -OH, -CH<sub>2</sub>OH, or -(CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>);

where R<sub>54</sub> and R<sub>55</sub> being the same or different are selected from -H, C<sub>1</sub>-C<sub>6</sub> alkyl, allyl, or phenyl (optionally substituted with 1, 2 or 3 -halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy or -CF<sub>3</sub>), or taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl, -4-(1-C<sub>1</sub>-C<sub>6</sub>alkyl)piperazinyl;

R<sub>41</sub> and R<sub>42</sub>, being the same or different, are selected from -H and C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>12</sub> is selected from -H, C<sub>1</sub>-C<sub>6</sub> alkyl, -C<sub>3</sub>-C<sub>6</sub> cycloalkyl, -CN, -C(O)NH<sub>2</sub>, -C(O)N(C<sub>1</sub>-C<sub>6</sub>alkyl)(C<sub>1</sub>-C<sub>6</sub>alkyl), -  
5 CO<sub>2</sub>H, -CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub>alkyl), -CH<sub>2</sub>OH, -CH<sub>2</sub>NH<sub>2</sub> or -CF<sub>3</sub>;

R<sub>13</sub> is selected from -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -CF<sub>3</sub>;

Y is selected from -S-, -S(O)-, -S(O)<sub>2</sub>, or -O-;

R<sub>4</sub> is -OH;

R<sub>5</sub> is selected -H, -C<sub>2</sub>H<sub>4</sub>OH, -C<sub>2</sub>H<sub>4</sub>-O-TBDMS, halo, -C<sub>3</sub>-  
10 C<sub>6</sub> cycloalkyl, C<sub>1</sub>-C<sub>3</sub> alkoxy, -CH<sub>2</sub>CH<sub>2</sub>Cl or C<sub>1</sub>-C<sub>4</sub> alkyl, with the proviso that R<sub>5</sub> is not isobutyl;

or, when R<sub>6</sub> is hydroxyl, R<sub>4</sub> and R<sub>5</sub> are taken together to form a five or six-membered saturated or unsaturated ring which together with the pyrimidine ring form the group  
15 consisting of 7H-pyrrolo[2,3-d]pyrimidine, 5,6-dihydro-7H-pyrrolo[2,3-d]pyrimidine, furo[2,3-d]pyrimidine, 5,6-dihydro-furo[2,3-d]pyrimidine, thieno[2,3-d]pyrimidine, 5,6-dihydro-thieno[2,3-d]pyrimidine, 1H-pyrazolo[3,4-d]pyrimidine, 1H-purine, pyrimido[4,5-d]pyrimidine,  
20 pteridine, pyrido[2,3-d]pyrimidine, or quinazoline, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C<sub>1</sub>-C<sub>6</sub> alkyl C<sub>1</sub>-C<sub>6</sub> alkoxy, -OH, -CH<sub>2</sub>OH, or -(CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>), -C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -CF<sub>3</sub>, -halo, -CO<sub>2</sub>(R<sub>31</sub>), -CON(R<sub>31</sub>)(R<sub>32</sub>), -CO(R<sub>31</sub>), -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(CO(R<sub>33</sub>)), -  
25 (CH<sub>2</sub>)<sub>n</sub>N(R<sub>31</sub>)(SO<sub>2</sub>(R<sub>33</sub>)), and the saturated ring may be optionally substituted with 1, 2 or 3, -C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -OH, -CH<sub>2</sub>OH, or -(CH<sub>2</sub>)<sub>n</sub>-N(R<sub>31</sub>)(R<sub>32</sub>) or one oxo (=O);  
and

R<sub>6</sub> is selected from -H, -OH, halo, -CN, -CF<sub>3</sub>, -  
30 CO<sub>2</sub>(R<sub>61</sub>), -C(O)R<sub>61</sub> or -C(O)N(R<sub>61</sub>)(R<sub>62</sub>) where R<sub>61</sub> and R<sub>62</sub> are the same or different and are selected from

-H,

C<sub>1</sub>-C<sub>6</sub> alkyl,

phenyl optionally substituted with 1, 2 or 3 -halo,

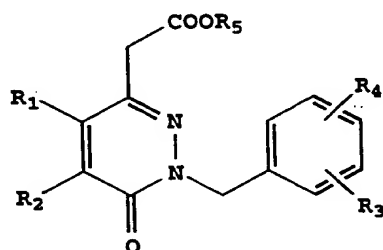
35 C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -CF<sub>3</sub>, -OH, -CN,

or where R<sub>61</sub> and R<sub>62</sub> taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -

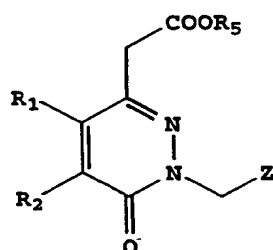
piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl, or -4-(C<sub>1</sub>-C<sub>6</sub> alkyl)piperazinyl;

pharmaceutically acceptable salts, hydrates, N-oxides and solvates thereof;

5 (XVII) compounds which have the structure



XVIIA



XVIIIB

where R<sub>1</sub> and R<sub>2</sub> are H, alkyl, aryl or arylalkyl, where the alkyl can include as substituents halogen, CF<sub>3</sub>, CH<sub>3</sub>O, CH<sub>3</sub>S, NO<sub>2</sub>, or R<sub>1</sub> and R<sub>2</sub> with the carbons to which they are attached can form methylenedioxy, or

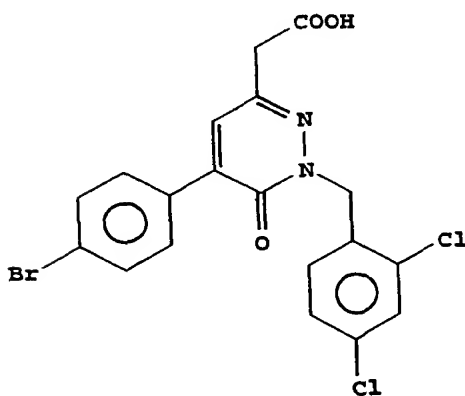
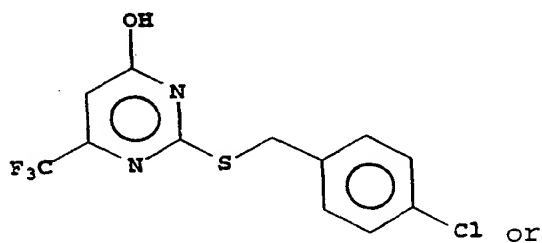
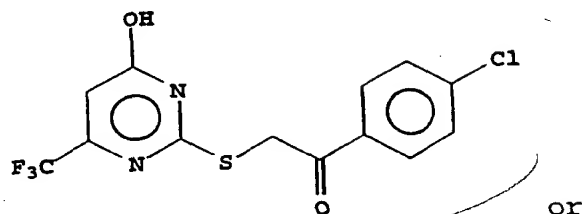
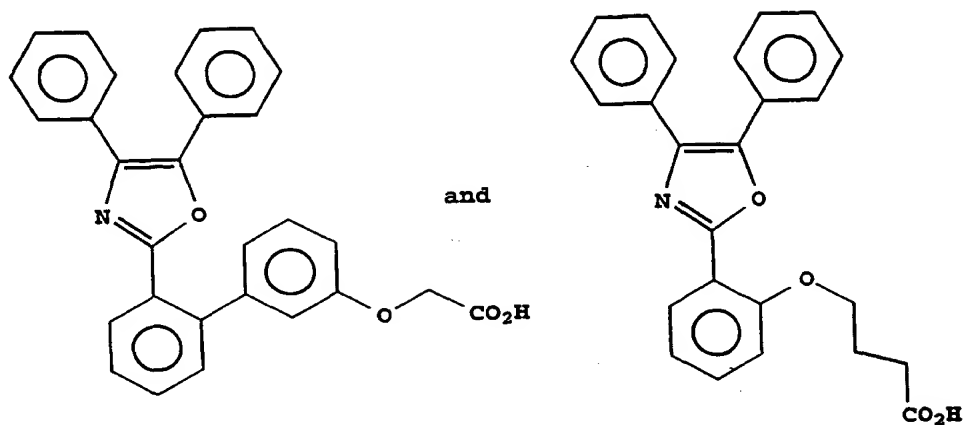
R<sub>1</sub> and R<sub>2</sub> can form a C<sub>3</sub>-C<sub>7</sub> non-aromatic ring, or a heterocycle which can be pyridine, pyrazine, pyrimidine, pyridazine, indol, or pyrazole, or an oxygen containing heterocycle which can be pyran or furan, or a sulfur containing heterocycle which can be thiopyran, or thiophene; the heterocycles being optionally substituted with halogen or alkyl,

R<sub>3</sub> and R<sub>4</sub> are H, alkyl, halogen, CF<sub>3</sub>, CH<sub>3</sub>O, CH<sub>3</sub>S or NO<sub>2</sub> or R<sub>3</sub> and R<sub>4</sub> with the carbons to which they are attached can form a methylenedioxy group,

R<sub>5</sub> is H, and

Z is a heterocycle which can be pyridine, thiazole, benzothiazole, benzimidazole or quinoline, which Z group can optionally be substituted with halogen or alkyl.

15. The method as defined in Claim 1 wherein the aP2 inhibitor has the structure



16. A pharmaceutical combination comprising an aP2 inhibitor and another type antiatherosclerotic agent.

17. The combination as defined in Claim 16 wherein the other antiatherosclerotic agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, other cholesterol lowering agent, a lipoxxygenase inhibitor, an ACAT inhibitor or a PPAR  $\alpha/\gamma$  dual agonist.

18. The combination as defined in Claim 16 wherein the antiatherosclerotic agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin or fluvastatin.

19. The combination as defined in Claim 16 wherein the aP2 inhibitor is present in a weight ratio to the antiatherosclerotic agent within the range from about 0.01 to about 100:1.

20. A method for treating atherosclerosis which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a pharmaceutical combination as defined in Claim 16.

09905235.074304  
TOCT 20 SE250660